wherein one or more tyrosine residues are phosphorylated based on the activation of signal transduction pathway, the extracellular domain of said receptor is capable of binding to its receptor ligand, and said ligand is generated from a precursor of said ligand by a proteinase-dependent cleavage;

contacting said cell with a compound affecting an extracellular G protein or G protein coupled receptor initiated signal pathway resulting in the activation of the receptor tyrosine kinase and thereby modulating the receptor tyrosine kinase activation by G-protein mediated signal transduction.

REMARKS

In further response to the Office Action dated May 21, 2002, attached are abstracts of references and data which show that the claims are enabled as presently written.

Applicants respectfully contend that the present invention is useful for receptor tyrosine kinases other than the EGF receptor. The references Kotecha et al., Waters et al., Bogulawski et al., Oak et al., Saito and Berk, Rueda et al., Heeneman et al., Miura et al., Tanimoto et al., Lee et al., Belcheva et al., Peng et al., and Sumitomo et al. (abstracts attached), demonstrate that G-protein or GPCR mediated transactivation not only takes place with EGFR, but also with other receptor tyrosine kinases such as PDGFR, KDR/FLK-1, TRK receptor, fibroblast growth factor receptor 1 and IGFR-1. All of these references were published in 2001 and 2002 and reflect the impact of the scientific achievement of the present invention, wherein the connection between G-protein/GPCR mediated signal transduction and transactivation of receptor tyrosine kinases has been elucidated for the first time.